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IN THE FOOD AND DRUG ADMINISTRATION

Comments on "Applications for FDA Approval to Market a New Drug: Patent Listing Requirements and Application of 30-Month Stays on Approval Of Abbreviated New Drug Applications Certifying That a Patent Claiming a Drug Is Invalid or Will Not Be Infringed" (67 Fed. Reg. 65448 (October 24, 2002))	Docket No. 02N-0417

Comments on Patent Listing and 30-Month Stay Proposals Submitted by the Generic Pharmaceutical Association (GPhA)

December 23, 2002

I. INTRODUCTION

On October 21, 2002, President Bush, in a Rose Garden ceremony, announced a proposal to close loopholes in the Drug Price Competition and Patent Term Restoration Act of 1984 (hereinafter "Hatch-Waxman"). The goals of this proposal, the President stated, were to promote fair competition in the pharmaceutical arena and thereby to reduce the cost of prescription drugs in America. In underscoring the need for action, the President emphasized that generic drugs are "just as safe and effective" as their brand counterparts and that they "make American health care far more affordable." President George W. Bush, Remarks by the President on Prescription Drugs (October 21, 2002), *available at* http://www.whitehouse.gov/news/releases/2002/10/20021021-2.html.

The President also recognized that "[c]urrent federal law and regulations attempt to carefully balance the goals of innovation and accessibility" and that "[b]oth of these goals [] are possible." Significantly, however, the President observed that, "*unfortunately, the careful balance of [Hatch-Waxman] is being undermined.*" *Id.* at 2 (emphasis added). Citing the recent report of the Federal Trade Commission,[1] the President stated that "some brand name drug manufacturers may have manipulated the law to delay the approval of competing generic drugs." *Id.* at 2. Specifically, the President noted that:

> When a drug patent is about to expire, one method some companies use is to file a brand new patent based on a minor feature, such as the color of the pill bottle or a specific combination of ingredients unrelated to the drug's effectiveness. In this way, the brand name company buys time through repeated delays, called automatic stays that freeze the status quo as the legal complexities are sorted out. . . . *In the meantime, the lower-cost generic drug is shut out of the market.*

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[1] Federal Trade Commission, "Generic Drug Entry Prior to Patent Expiration: An FTC Study" (July 2002), *available at* http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf (hereafter, "FTC Report").

See President Bush's Remarks at 2 (emphasis added).

The President's proposal would amend the Food and Drug Administration's regulations to restore the Hatch-Waxman balance. *See* "Applications for FDA Approval to Market a New Drug: Patent Listing Requirements and Application of 30-Month Stays on Approval of Abbreviated New Drug Applications Certifying That a Patent Claiming a Drug Is Invalid or Will Not Be Infringed," 67 Fed. Reg. 65448 (proposed October 24, 2002) (to be codified at 21 C.F.R. pt. 314). The Administration's regulatory proposal is the subject of these comments by the Generic Pharmaceutical Association ("GPhA").

II. SUMMARY

As the President observed, the challenge before this nation is "to increase access to quality care, while preserving the finest health care system." In order to achieve this goal, essential steps must be taken to make critical drugs more affordable for every American. This means that anticompetitive tactics and other market barriers must not be permitted to block consumer access to affordable generic pharmaceuticals. Affordable medicines allow patients and health care providers to ensure quality of care while preserving precious financial resources -- resources that could be better used to support other healthcare benefits, to maintain current premiums, or to simply preserve benefits currently offered.

As the Vice-President recognized in his statement three days after the President's announcement, the current Hatch-Waxman process must be "made more efficient and fair, so generic medicines become available as quickly as possible," and "[b]y reducing the public's wait for generic drugs, we'll reduce the cost of prescriptions in this country by billions of dollars." Vice-President Richard Cheney, Remarks at Event for Florida State Senator Brown-Waite (Oct. 24, 2002).

GPhA and its members wholly endorse the President's message that measures must be taken to ensure timely access to affordable pharmaceuticals. GPhA applauds the President, Vice-President, and FDA for recognizing the importance of fostering pharmaceutical drug competition, and for proposing measures to address anticompetitive conduct that has permeated the Hatch-Waxman system in recent years to the detriment of American consumers and health care providers.

As we will explain in more detail below, FDA's proposed rule contains certain measures that, if amended as GPhA suggests, could help prevent brand companies from using loopholes in the Federal Food, Drug, and Cosmetic Act ("FFDCA") and implementing regulations to block generic competition. GPhA respectfully submits that the FDA's proposals to clarify the criteria for patent listing eligibility and to require enhanced patent listing declarations could significantly limit current abuses in the patent listing process, provided that the proposals are modified as proposed below and are effectively policed by the FDA and FTC.

FDA's proposal to limit brand companies to a single 30-month stay per ANDA could, however, cause further imbalance in the Hatch-Waxman system by impeding the ability of generic companies to obtain timely resolution of legitimate patent disputes. GPhA agrees with FDA and FTC that Congress never intended that brand companies could game the Hatch-Waxman system by obtaining multiple 30-month stays of generic drug approvals. GPhA also agrees that eliminating this kind of gaming is an important objective of any reform effort. However, truly effective Hatch-Waxman reform not only must prevent gaming of the Hatch-Waxman system; it must also ensure early resolution of legitimate patent disputes between generic and brand companies, so that these disputes are resolved and generic drugs may go to

market as quickly as possible.[2] The twin goals of preventing gaming of the Hatch-Waxman system and ensuring timely resolution of brand-generic patent disputes are completely reconcilable. And both goals must be achieved concurrently if the Hatch-Waxman balance is to be fully restored.

While we applaud the intent behind the Agency's 30-month stay proposal, this proposal actually may *make it easier* for brand companies to delay bringing litigation against generic companies that have applied for FDA approval of their products. The 30-month stay functions as the principle incentive for brand companies to participate in the expedited Hatch-Waxman process. Partial removal of that incentive, as proposed by the FDA, without the addition either of new incentives or public policy mandates requiring brand companies to list patents in the Orange Book and to initiate timely litigation on those patents, will encourage brand companies to act later, rather than sooner, to protect their patents. Thus, in serving one of the key goals of Hatch-Waxman reform (prevention of gaming), the partial removal of the 30-month stay *disserves* a fundamental principle of Hatch-Waxman (early resolution of patent disputes). These twin goals must be implemented in tandem if the goals of the Administration are to be achieved. Implementation of one without the other could undermine the Administration's objectives.

Moreover, in addition to potentially delaying resolution of legitimate patent disputes – a result that would cost this Nation billions of dollars -- the proposed 30-month stay provisions might also have other adverse effects on the Hatch-Waxman balance. In particular, the proposed rule also leaves untouched certain existing forms of brand company abuse, such as late, frivolous

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[2] For purposes of the comments, a "legitimate" patent dispute is a dispute over a patent that meets the statutory criteria for Orange Book listing and that presents significant corporate exposure to the generic company which must be eliminated prior to product launch.

patent listings where previous brand patents were not challenged. The proposed rule also may weaken other essential aspects of Hatch-Waxman, such as 180-day generic exclusivity – the principle incentive for generic companies to challenge questionable brand company patents.

In summary, effective Hatch-Waxman reform requires a comprehensive approach, in which no single component of the system is viewed in isolation. Rather, much like a complex mathematical equation, Hatch-Waxman reform must be assessed and undertaken as a whole to determine whether the entire system will yield the desired outcome of timely access to affordable medicine. GPhA recognizes that there are limits on FDA's statutory authority that preclude the Agency from undertaking a comprehensive Hatch-Waxman reform effort. To this end, GPhA submits that to make American health care more affordable, legislative reform that encompasses the twin goals of preventing gaming of the Hatch-Waxman system *and* ensuring that brand companies act quickly to list and litigate their patents is the only viable option.[3] The Agency's proposal to limit the 30-month stay provision, while well-intentioned in its effort to address the anticompetitive effects of frivolous patent listings, unfortunately fails to effectuate the Administration's stated objective of restoring the Hatch-Waxman balance and, therefore, should

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[3] Throughout its dialogue with FDA in the past year, GPhA has consistently argued that administrative changes are inadequate to fix the Hatch-Waxman system. *See, e.g.,* January 18, 2002 Letter from GPhA to Daniel Troy ("The system begs for a more thorough reform than is possible through simply revising existing regulations and policies.") *available at* http://www.fda.gov/cder/ogd/GPHA_Jan_21.htm. This letter is attached hereto as Exhibit A. During the past year, the inadequately of administrative solutions and the need for legislative reform has become even clearer to GPhA. In fact, as demonstrated in these comments, even well-intentioned regulatory reform, such as the Agency's proposal to address abuses of the 30-month stay provision, may create more problems than it solves.

not be implemented.[4]

Section III of these comments provides an overview of the Hatch-Waxman regime. Section IV describes the recent abuses of Hatch-Waxman by brand companies. Section V addresses the proposed rule's patent listing and Orange Book provisions. And Section VI addresses the 30-month stay provisions of the proposed rule.

III. BRIEF OVERVIEW OF HATCH-WAXMAN

As discussed above, a principal goal of Hatch-Waxman is to ensure the entry into the market of affordable generic drugs as soon as brand company patent protections expire or are defeated in court.[5] In aid of this goal, the Amendments set forth a process for the identification and litigation of brand-name patents, so that patent disputes between generic and brand-name companies can be resolved early and quickly.[6] Swift resolution of patent disputes, in turn, gives generic companies the certainty they need before they can proceed to market.

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[4] Should FDA nevertheless decide to finalize the proposed rule in its current form, GPhA members believe that the Agency should adopt an interpretation of the rule that would *permit*, but not *require*, generic applicants to provide brand companies with a notice that can trigger a 30-month stay. While this interpretation may still be fraught with problems, it would at least restore some of the incentive that is necessary for the early resolution of legitimate patent disputes.

[5] *See* H.R. Rep. No. 98-857, pt. II (1984) *reprinted in* 1984 U.S.C.C.A.N. 2716-17 (declaring that one of the principal policy objectives of Hatch-Waxman was to "get[] safe and effective generic substitutes on the market as quickly as possible after the expiration of a patent."); *In re Barr Labs., Inc.*, 930 F.2d 72, 76 (D.C. Cir. 1991) (finding that a purpose of Hatch-Waxman was to "get generic drugs into the hands of patients at reasonable prices – *fast*") (emphasis added)).

[6] *See* 67 Fed. Reg. at 65448 (Hatch-Waxman "promotes competition [between generic and brand-name drugs] by creating a process to expedite the filing and approval of ANDAs . . . and for resolving challenges to patents before marketing begins.")

The interaction between the patent law and generic drug pricing make it especially critical to generic manufacturers that the status of legitimate brand company patents be resolved before the generic begins marketing. Because generic drug prices are up to 70 percent lower than brand drug prices, the profits *earned* by a generic company for sales of its drug product are substantially less than the profits *lost* by the brand company when the generic product improperly takes a sale away from the brand company. Under the patent laws, an infringer is liable to the infringee for the latter's lost profits – not simply for the profits earned by the infringer. In the case of a so-called "blockbuster drug," the difference between the generic company's earned profits and the brand company's lost profits can be in the hundreds of millions of dollars. Further, if the generic is found to have acted in willful disregard of the patentee's rights (in patent parlance), those lost-profits damages could be trebled.

Given the potential for these kinds of damage awards, generic companies cannot assume any significant risk of incurring lost-profits damages, let alone treble damages. For this reason, generic companies have rarely ever marketed a product before resolving legitimate patent disputes with the brand company. And for this reason, significant uncertainty about patent liability will likely prevent generic companies from launching any affordable products.

Hatch-Waxman is designed to eliminate this uncertainty early in the process. Specifically, the statute creates a framework for patent litigation to proceed concurrently with the FDA's consideration of the generic ANDA, so that the generic company, if it prevails in court, may go to market as soon as possible, free of the risk of lost profits and treble damages. The Hatch-Waxman system works as follows.

First, a brand company that files a new drug application (NDA) must provide FDA with information regarding certain patents relating to the drug that is the subject of the NDA. Upon

approval of the NDA, a patent relating to the approved drug may be listed in the Orange Book if it meets two statutory criteria: (1) the patent must "claim[]" the drug product, or a method of using the drug product, for which the brand company submitted the NDA; and (2) an assertion of patent infringement must be able to be reasonably asserted if an unlicensed person engages in the manufacture, use or sale of that product. 21 U.S.C. § 355(b)(1) (2001). *Only* patents that meet these criteria are eligible for an Orange Book listing. *Pfizer, Inc. v. FDA*, 753 F.Supp. 171 (D. Md. 1990). The types of patents that are eligible for listing in the Orange Book include drug substance patents (which cover the active ingredient in the drug product); method of use patents (which cover the use of the product to prevent, treat, or diagnose certain health problems); and drug product patents (which cover the physical composition or delivery mechanism of the drug product). Process patents, which cover the procedure used to make the active ingredient or the drug product, may not be listed in the Orange Book. 21 C.F.R. § 314.53(b) (2002).

Second, when FDA approval is sought for a generic version of an Agency-approved brand drug, the generic company must file an Abbreviated New Drug Application ("ANDA") in which, among other things, it responds to each patent listed in the Orange Book on behalf of the FDA-approved brand drug. The ANDA applicant must certify for every such patent one of the following:

(I) The patent information has not been submitted to FDA;

(II) The patent has expired;

(III) The patent will expire on a particular date prior to marketing of the generic product; *or*

(IV) The patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the product for which the ANDA is submitted.

21 U.S.C. § 355(j)(2)(A)(vii) (2001).[7] A generic company that certifies under Paragraph IV must notify the patent holder of its intent to challenge the patent. 21 U.S.C. § 355(j)(2)(B) (2001).[8] The ANDA applicant's filing of a Paragraph IV certification and its notice of the certification to the patent holder triggers the patent holder's right to bring a patent suit against the ANDA applicant under Title 35, United States Code. A brand company has 45 days from receipt of notice of a Paragraph IV certification to bring its patent infringement suit. 21 U.S.C. § 355(j)(5)(B)(ii) (2001). If such a suit is filed, Hatch-Waxman provides that the generic company's ANDA may not be approved for 30 months, or until a court has resolved the patent dispute, whichever occurs first. *Id.*

In essence, the 30-month stay is equivalent to an automatic preliminary injunction against the generic company and the FDA. This stay allows brand companies to reap additional and unnecessary monopoly benefits beyond those granted by the patent system and therefore is of great value to eligible brand companies. Because the 30-month stay can only be triggered by litigation brought in response to a notice filed by an ANDA applicant regarding a Paragraph IV certification to an Orange Book-listed patent, the stay also serves as an incentive to brand

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[7] A nearly identical patent certification provision also applies to NDAs filed under section 505(b)(2) that rely on studies not conducted by the applicant but which are not eligible for a ANDA under section 505(j). *See* 21 U.S.C. § 355(b)(2)(A) (2001). For simplicity, these comments refer to ANDAs; however, we note that the patent dispute and 30-month stay provisions discussed below also apply to applications filed pursuant to section 505(b)(2). *See* 21 U.S.C. §§ 355(b)(3), (c)(3) (2001).

[8] Generic companies have an incentive to undertake the cost of challenging potentially invalid or uninfringed patents because Hatch-Waxman provides that a generic patent challenger is entitled to 180 days of its own marketing exclusivity. 21 U.S.C. § 355(j)(5)(B)(iv) (2001).

companies to operate within the expedited Hatch-Waxman framework, and not to delay enforcing their patents until the end of the ANDA approval process.

A patent ineligible for listing in the Orange Book cannot be the subject of a 30-month stay, nor can it legally preclude FDA from approving competing drug products. Holders of patents that are ineligible for Orange Book listing, however, retain the same intellectual property rights under United States patent law and such patents can still be the basis for a conventional patent infringement suit against the generic company to prevent marketing. In such cases, however, in order to block marketing of the generic drug during the pendency of the suit, the brand company must obtain a preliminary injunction against the alleged infringer, 35 U.S.C. § 283 (2001). Such an injunction is available only if the brand-name company meets the criteria applicable to other patent holders. *See Serono Labs. v. Shalala*, 158 F.3d 1313, 1317 (D.C. Cir. 1998) (setting forth preliminary injunction criteria).

IV. ABUSES OF THE HATCH-WAXMAN SYSTEM

A Hatch-Waxman automatic 30-month stay can provide an enormous financial windfall to a brand company in the form of two and one-half years of additional market exclusivity. Therefore, brand companies have a substantial incentive to position themselves to qualify for such stays. And since a 30-month stay may only be based on an Orange Book-listed patent, brand companies have "a considerable incentive to cause the FDA to list patents in the Orange Book." *Mylan Pharmaceuticals, Inc. v. Thompson*, 139 F.Supp.2d 1, 4-5 (D.D.C. 2001), *rev'd* 268 F.3d 1323 (Fed. Cir. 2001). These incentives have caused some brand companies, particularly in recent years, to "game" the Orange Book listing/patent dispute process in order to extend brand company product monopolies beyond what Congress intended when it enacted the Hatch-Waxman Amendments. These efforts have directly undermined the statute's goal of

affording swift, public access to affordable generic drugs immediately after the expiration of a finite period of brand company intellectual property protection.

Brand company manipulation of the patent listing/dispute process can take several forms. First, because an Orange Book-listed patent is a precondition to obtaining a 30-month stay, some brand companies have increasingly listed patents in the Orange Book that relate to approved drugs but that do not meet the statutory or regulatory listing criteria – *e.g.*, patents that do not claim the approved drug product, or an approved use of that drug product, or that do not give rise to a reasonable claim of patent infringement. Given FDA's position that it should have no role in overseeing the Orange Book listing process, which we discuss in greater detail below, the improperly listed patent can obtain a 30-month stay and the resulting automatic extension of the brand-name monopoly.

Moreover, some brand companies are increasingly timing their Orange Book listings to obtain unwarranted extensions of their market exclusivity. For example, some brand companies have resorted to listing patents in the Orange Book *after* the filing of an ANDA. Under FDA's regulations, a later-issued patent (*i.e.*, listed in the Orange Book after ANDA filing) requires a supplemental certification and notice to the NDA holder by the ANDA sponsor which, in turn, triggers the statute's 30-month stay provisions. If one 30-month stay is already in place due to the generic company's Paragraph IV certifications in its original ANDA, the listing of a later-issued brand company patent generates a second 30-month stay against the generic. Thus, just as patent litigation occasioned by a pre-ANDA Orange Book listing is about to reach its conclusion, and as the first 30-month stay on the ANDA is about to expire, a generic company will face another 30-month barrier to market entry. Such eleventh-hour patent listings are, of course, improper when the patent does not meet the statutory or regulatory listing criteria. Even where

the eleventh-hour patent does qualify for listing, however, the brand company's timing of the patent listing in order to obtain a second 30-month extension of its product monopoly can undermine the goals of Hatch-Waxman.

The FTC's recent report thoroughly reviewed these practices and concluded that some brand companies have improperly blocked generic competition. The FTC report examined brand company efforts to use the 30-month stay provisions to extend their product monopolies, and found that these efforts had increased in recent years. For example, while brand companies only listed two patents in the Orange Book after the filing of an ANDA between 1992 and 1998, they listed six such patents in 1999-2000. *FTC Report* at iii. In seven of the eight cases involving later-issued patents, these patents triggered 30-month stays after initial stays had already been triggered by Paragraph IV certifications in the original generic ANDAs. In these seven cases, the brand companies received between four and 40 months of additional market exclusivity, in addition to the first 30-month stay, which translates into between 34 and 70 months of delay. *Id.*[9] Moreover, the FTC determined that "most of the later-issued [*i.e.*, post-ANDA] patents in the Orange Book raise questions about whether the FDA's patent listing requirements have been met. For example, many do not appear to claim the approved drug product or an approved use of

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[9] The FTC concluded that each of these eight cases involved a "blockbuster drug" – *i.e.*, one of the handful of drugs that generate a disproportionate percentage of brand-name company profits. Indeed, four of the eight brand-name drugs that enjoyed additional exclusivity as a result of a late issued patent achieved net sales of over $500 million in the year of additional exclusivity, and all of the eight drugs enjoyed sales over $100 million in those years. *FTC Report* at 49 (Table 4-3). The motivation behind brand company efforts to extend their product monopolies in these cases is clear, as are the tremendous negative effects on America's consumers.

the drug," as plainly required by Hatch-Waxman.[10] *Id.* at 40. Indeed, in the four cases where a court has decided the validity of a later-issued patent, the court has found, in each case, that the relevant patent was either invalid or not infringed. *Id.* at iv.

In short, the FTC has expressly found that some brand companies have manipulated the Orange Book listing and 30-month stay provisions of Hatch-Waxman to improperly extend their product monopolies and to undermine the goals of the statute. FDA has acknowledged the FTC Report's conclusions in its notice of proposed rulemaking. 67 Fed. Reg. at 65449. Indeed, FDA determined that the FTC Report "addressed multiple stays in the context of a limited number of 'blockbuster' drugs" and that "[t]he total number of stays in ANDA approvals is higher . . . ." *Id.* at 65449.

As the FTC noted, brand manipulation of the Hatch-Waxman system is made possible, in part, by FDA's refusal to review Orange Book listings and by the lack of a mechanism by which generic companies or others may challenge the validity of such a listing. *FTC Report* at 44. FDA has taken the position that it lacks the expertise and resources to review the "listablility" of a patent and has declined to enact a procedure for resolving listing disputes.[11] The only action that a brand company must take to qualify for an Orange Book listing is to submit a brief certification to FDA stating that the listing criteria have been satisfied. 21 C.F.R. § 314.53(c)(2)

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[10] "A patent 'claims' a product only when the written section of the issued patent labeled 'claims' define it." *FTC Report* at 54, *citing Hoechst-Roussel Pharms., Inc. v. Lehman*, 109 F.3d 756 (Fed. Cir. 1997).

[11] *See* 59 Fed. Reg. 50338, 50343 (Oct. 3, 1994) ("FDA does not have the expertise to review patent information. The agency believes that its resources would be better utilized in reviewing applications rather than reviewing patent claims."); 54 Fed. Reg. 28872, 28910 (July 10, 1989) ("In deciding whether a claim of patent infringement could reasonably be asserted . . . the agency will defer to the information submitted by the NDA applicant.").

(2002). And if a generic company disputes the listability of the patent, FDA's practice is simply to permit the proponent of listing recertify to the correctness of its original certification. 21 C.F.R. 314.53(f) (2002). This policy has been upheld by the courts as within FDA's administrative discretion. *AaiPharma v. Thompson*, 2002 WL 1473429 (4th Cir. July 10, 2002); *Watson Pharmaceuticals v. Henney*, Civil Action No. 00-3516 (D. Md. January 17, 2001).

In the absence of any oversight of the listing process, a generic company that questions the listability of a patent must make a Paragraph IV certification against the patent – which, in turn, triggers the Hatch-Waxman 30-month stay of the generic ANDA, automatically delaying the public's access to affordable medicines. As noted in the FTC Report, several generic applicants have sought court orders requiring FDA or brand-name companies to delist certain patents from the Orange Book and thereby freeing the generic company from the 30-month stay related to that patent. *FTC Report* at 44. The courts, however, have held that there is no private right of action for delisting under the FFDCA. *See Andrx Pharm., Inc. v. Biovail Corp.*, 276 F.3d 1368 (Fed. Cir. 2002); *Mylan Pharm., Inc. v. Thompson*, 268 F.3d 1323 (Fed. Cir. 2001). While the United States Court of Appeals for the Federal Circuit has suggested that an ANDA applicant may sue FDA under the Administrative Procedures Act for failure to delist an improperly listed patent, this suggestion is contrary to FDA's policy that it will not examine the listability of an Orange Book patent, and any such challenge would have to survive the Administrative Procedure Act's deferential standard of judicial review.

V. REFORM OF THE PATENT LISTING PROCESS

The proposed rule addresses improper Orange Book listings in two ways. First, it amends its patent listing regulations to clarify what types of patents may be legitimately listed in the Orange Book. Second, it proposes a declaration that the Agency would require to be

submitted in conjunction with a listing request. The purpose of the declaration is to require Orange Book listing proponents to systematically determine whether their patents in fact qualify for listing under the FFDCA and its implementing regulations.

The proposed rule attempts to bring greater accountability and clarity to the Orange Book listing process and could significantly limit current abuses of that process. If the rule is to achieve its full effect, however, certain modifications to FDA's current approach are necessary, especially with respect to the Agency's treatment of product-by-process patents and polymorphs and with respect to the enforcement of the Orange Book listing criteria.

A. Clarification of Patents That May Be Listed in the Orange Book

The proposed rule amends the patent listing regulation (21 C.F.R. § 314.53(b)) to clarify that certain types of patents may be listed in the Orange Book and that other types of patents may not.

GPhA strongly supports FDA's amendment of its regulations to clarify that patents claiming metabolites, patents claiming packaging, and patents claiming intermediates are ineligible for listing in the Orange Book. 67 Fed. Reg. at 65464. However, GPhA strongly opposes FDA's proposal to amend its regulations to state that patents claiming a different, but therapeutically equivalent, form of the approved drug substance (referred to hereafter as "polymorph" patents) and "product-by-process" patents must be listed in the Orange Book. FDA's proposal regarding polymorphs, in particular, is directly contrary to law, represents a reversal of FDA's previous position, and thoroughly contradicts FDA's announced desire to help restore the Hatch-Waxman balance. As to both product-by-process patents and polymorphs, FDA's approach represents a departure from the FTC's analysis of the listing

issues. GPhA wholly endorses the FTC approach and urges FDA to withdraw these portions of its proposed rule.

1. Polymorph Patents

FDA's proposal to require brand companies to list polymorph patents in the Orange Book in cases where the FDA-approved drug is not the polymorph form of the product is directly contrary to the FFDCA's patent listing requirements and United States patent law. As the FTC has recognized, a patent that "claims" an unapproved polymorph version of a drug product cannot be said under either the FFDCA or the patent law to "claim" the approved drug product and therefore cannot be listed in the Orange Book. FDA's approach to polymorphs is directly contrary to the FTC's correct statutory interpretation, which GPhA endorses, and, if implemented, this proposal would give brand companies a new opportunity to use 30-month stays to improperly block generic competition. In short, FDA's proposal on polymorphs would undermine the goals of Hatch-Waxman and should be withdrawn.

Under the FFDCA, only a "patent which *claims* the drug . . . or which *claims* the method of using such drug" may be submitted to FDA for listing in the Orange Book. 21 U.S.C. §§ 355(b)(1), (2) (2001) (emphasis added). Polymorphs are different forms of the same drug substance. For purposes of this discussion, a polymorph patent is a patent that claims a different, unapproved form of an approved drug substance. For example, if FDA approves an anhydrous (no water molecule) form of a drug substance, but a patent claims a monohydrate (one water molecule) form of the substance, the patent is a polymorph patent. The proposed rule would amend FDA's regulations to explicitly expand current patent listing criteria to include polymorph patents – *i.e.*, a different form -- of an approved drug product.

As FDA itself acknowledges in the preamble to the proposed rule, the proposal to permit the listing of polymorph patents in the Orange Book conflicts with the Agency's longstanding position that a patent must claim the chemical form of the approved drug product to be listed in the Orange Book. 67 Fed. Reg. at 65452. A different, unapproved form of an approved active ingredient, as FDA recognizes in proposed rule, is different from the approved drug product, and, therefore, the FDA has historically taken the position that polymorph patents are ineligible for Orange Book listing. *Id.* at 65452. FDA's current assertion that a patent may "claim" an approved drug substance when it is in a different form from that approved substance is contrary to law.

More specifically, the Agency's reading of "claims" thoroughly ignores the meaning of that term in the patent law, whence the term is derived, and in the FFDCA. As the FTC recognized, "claims" is a term of art that specifically refers to the practice of defining a product in the "claims" section of the patent. *See Mylan Pharma., Inc. v. Thompson*, 139 F.Supp. 2d 1, 19-21 (D.D.C. 2001) (interpreting "claims" language of listing statute *in pari materia* with language in patent restoration section of Hatch-Waxman Act), *rev'd on other grounds*, 268 F.3d 1323 (Fed. Cir. 2001). A patent that does not "claim" a particular product, or a bioequivalent version thereof, may still be infringed by that product (*see FTC Report* at 54 (describing types of infringement where patent does not claim product)); but the possibility of infringement is irrelevant to the listing analysis if the specific definition of "claims" is not met. As the Federal Circuit has noted, "the plain meaning of 'claims' is not the same as the plain meaning of infringement." *Hoechst-Roussel Pharms., Inc. v. Lehman*, 109 F.3d 756, 759 (Fed. Cir. 1997). FDA's proposed rule ignores this basic principle of patent law and in so doing, permits the

listing of patents contrary to the explicit requirement of the FFDCA that only patents which "claim" the drug that is covered by the NDA may be listed.

FDA explains its departure from its previous position and from the requirements of the FFDCA and patent law by comparing its treatment of polymorphs in the Orange Book context to its treatment of polymorphs for purposes of determining *therapeutic equivalence*. Drug products containing different forms of the same active ingredient, including a polymorph form of an approved drug, may be found to be therapeutically equivalent and therefore may be the subject of an ANDA. *See Serono Lab.*, 158 F.3d at 1320-1322 (upholding an FDA interpretation of "same" under 21 U.S.C. § 355(j) as not requiring a generic drug to be chemically identical to its brand counterpart in all respects). The Agency therefore reasons that if a patent for a polymorph of the approved brand product cannot be listed in the Orange Book, the generic company may not receive notice of the existence of a patent on the polymorph that forms the basis for its ANDA and might unknowingly infringe that patent.

FDA's analysis is flawed. The fact that a polymorph is therapeutically equivalent to an approved drug product does not change the fact that listing of polymorph patents is contrary to the FFDCA's patent listing criteria, which require that a patent "claim" an *approved drug product.* A polymorph patent claims a drug form that is different from the approved drug product and therefore cannot be listed in the Orange Book under the FFDCA, regardless of whether the form of the polymorph is therapeutically equivalent to the approved product. Thus, the proposed rule's treatment of polymorphs conflicts directly with the FFDCA.

As the FTC found, "[t]he key relationship governing whether a patent is properly listed in the Orange Book is the relationship between the patent and the brand-name drug product." *FTC Report* at 52. The fact that a polymorph may be therapeutically equivalent to an approved drug

product, and that a patent based on that polymorph may therefore be infringed by a generic version of that product, does not determine whether the polymorph patent meets the statutory criteria for listing in the Orange Book. Therapeutic equivalence and listability are unrelated concepts.[12]

Indeed, as the FTC noted in its report, "it is entirely possible, and in fact common, for a patent to claim the brand-name drug (and hence be listed in the Orange Book), but not to be infringed by a bioequivalent generic product" and at the same time also "possible for a bioequivalent generic product to infringe a patent that does not claim the brand-name drug (and hence should not be listed in the Orange Book.)" *Id.* at 52-53. See also *id.* at A27 (FTC Citizen Petition) ("the fact that the FDA may consider one chemical compound pharmaceutically equivalent to, or the same active ingredient as, another chemical compound for purposes of [Hatch-Waxman] does not alter the requirement of 21 C.F.R. § 314.53 that a listed drug substance patent must claim a component of an approved drug product.") In short, *"[t]he relationship between [a] patent and any bioequivalent generic drug is irrelevant to the listing question,"* *id.* at 52 (emphasis in original), and FDA cannot appropriately use therapeutic equivalence as a basis for the decision to permit listing of polymorphs.

FDA suggests that its rationale for equating listability and therapeutic equivalence is to ensure that generic companies will receive notice of polymorph patents. FDA's analysis ignores that fact that generic companies regularly conduct comprehensive due diligence efforts to assess

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[12] *See Serono Lab., supra* (noting that a generic version of the NDA-approved product need not be chemically identical to the brand product to meet the statutory definition of sameness).

corporate liability and market opportunities.[13] *See id.* at 54 ("The importance of the notice function of the Orange Book is unclear . . . Many companies may not need an Orange Book listing to provide notice, given the sophistication of their patent searching techniques and the common practice of monitoring newly listed patents on a daily basis.")[14] Any minimal benefit provided by such notice, if one exists at all, is far outweighed by the opportunity that such a change in policy would give brand-name companies to artificially obtain a 30-month stay by listing a late-filed patent that must be litigated before the generic product may be marketed. If the benefits of listing polymorphs are uncertain, the costs are clear: the listing of polymorphs would provide brand companies with yet additional opportunities to forestall generic competition and to undermine the goals of the Hatch-Waxman Amendments.

In summary, FDA's proposal to provide for the Orange Book listing of polymorph patents is contrary to the patent listing criteria of the FFDCA as well as to the goals of Hatch-Waxman, and GPhA urges the Agency to withdraw this portion of the proposed rule.

2. "Product-by-Process" Patents

As FDA notes, a true product-by-process patent claims a product by using or listing process steps to wholly or partially define the claimed product. *See In re Luck*, 476 F.2d 650 (C.C.P.A. 1973); *In re Brown*, 459 F.2d 531, 535 (C.C.P.A. 1972). In other words, in a product-by-process patent, the process used to make the product and the product itself are inextricably

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[13] Corporate patent due diligence efforts consist of, among other things, the identification and assessment of patent issued by Patent & Trademark Office (PTO) as well as patent applications pending before that agency.

[14] For example, generic companies perform due diligence investigations to identify patents either issued by the Patent and Trademark Office ("PTO") or pending before PTO that may affect their interests. 35 U.S.C. § 122 provides for pre-approval publication of patent applications 18 months after the earliest filing date, thereby enabling generic companies and other interested parties to review a patent application's contents before the patent is issued by PTO.

connected: the *only* way to describe the product is by describing the process, or, if the product is not new, by claiming a novel process-based limitation.

The FTC has made a convincing argument that the listing of such patents should not be permitted, noting that a product-by-process patent is a type of process patent and that process patents may not be listed under the FFDCA, as interpreted by FDA's regulations. *FTC Report* at A42-A43 (*citing* 21 C.F.R. § 314.53). But even if a true product-by-process patent, as described above, satisfies the listing criteria in the Orange Book, the problem is that in the pharmaceutical arena, brand companies have succeeded in disguising process patents, which are unlistable under FDA's interpretation of the statute, as product-by-process patents. Examples of this practice include a Paxil patent on paroxetine manufactured through dry compression tableting, and a process patent on Omeprazole listed to describe an unapproved polymorph(s). In such cases, brand name companies cannot claim a new chemical compound because the compound was already the subject of prior patents, and therefore resort to claiming a product-by-process formulation that is in fact merely a regular, unlistable process patent in disguise. Under current patent law, product-by-process patents issued by PTO are highly unlikely to claim a product.

Given the absence of product-by-process patents in the synthetic pharmaceutical area, and given the potential for abuse of the patent listing process by companies seeking to list "process patents in disguise," it would be irresponsible of FDA to expressly provide that product-by-process patents can be listed in the Orange Book, without providing guidance as to how to distinguish a true product-by-process patent from a simple process patent. FDA itself recognizes that the distinction is a difficult one to draw (67 Fed. Reg. at 65452), and it has invited comment on ways to ensure that only product-by-process patents are listed. In response to this invitation, GPhA suggests that the Agency use GPhA's proposed patent listing

declaration, which GPhA submitted to FDA in January 2002 and which is attached hereto as Exhibit B, to distinguish between product-by-process patents and mere process patents.

The GPhA proposed revised declaration contained a number of questions (questions C1-C4) designed expressly to expose whether an alleged product-by-process patent is actually a mere process patent in disguise. As drafted, the declaration included as part of the proposed rule does not include any questions on the issue of product-by process-patents. *See* 67 Fed. Reg. at 65453-54. Adding questions C1-C4 from GPhA's proposed declaration to FDA's proposed declaration would be one concrete way of addressing the concerns identified by the Agency in its Notice.

B. Lack of a Listing Review Mechanism

The proposed FDA rule provides no mechanism by which FDA may "delist" an Orange Book patent or refuse to list the patent in the first instance, or by which a generic company may challenge an Orange Book listing. As discussed above, and as made clear in the FTC Report, the improper listing of patents in the Orange Book is a common technique used by brand–name companies to delay generic competition. As the FTC Report noted, many of the patents that are the basis for 30-month stays, especially patents listed after the filing of an ANDA that are the basis of such stays, raised significant listability issues. *FTC Report* at 40 ("[M]ost of the later-issued patents in the Orange Book raise questions about whether the FDA's patent listing requirements have been met"). As long as 30-month stays remain available to brand companies (even if only one such stay is available per ANDA, as FDA proposes), these companies will have an incentive to list patents on the eve of generic competition, regardless of whether the patent meets the statutory/regulatory criteria. This is especially true in instances where the first listed brand patents are not challenged.

The current system has failed to deter this misconduct, as illustrated by current Orange Book listings relating to, among others, process and unapproved use patents. FDA has historically declined to review whether patents qualify for Orange Book listing, and courts have held that there is no private right of action to challenge an Orange Book listing. Legislative Hatch-Waxman reform proposals in the 107th Congress provided for challenges to a patent's listability. In the absence of legislative reform, however, it is incumbent on *FDA itself* to establish an administrative process by which the Agency will: (1) examine a patent to see whether it qualifies for Orange Book listing under the statute; and (2) delist the patent if it does not.

FDA has long claimed that the issue of whether a patent should be listed in the Orange Book is a matter of patent law and, therefore, implicates issues that are outside the sphere of its expertise. However, as the FTC Report noted, "[m]any of the listing issues concern the FDA's listing regulations . . . rather than interpretations of patent scope" and "the identification of individual patents as falling into one of th[e] categories [of listable patents] is usually relatively straightforward." *FTC Report* at 55; *see also id.* ("The question of whether a patent claims some unapproved aspect (and hence should not be listed) may depend more on an interpretation of the NDA's scope of approval than an interpretation of the patent.")

The dispute regarding Biovail Corp.'s high blood pressure brand drug Tiazac is an example of a listing dispute that fell directly within FDA's sphere of authority, but that the Agency failed to adequately address on grounds that it lacked patent expertise. *See Andrx Pharm., Inc. v. Biovail Corp.*, 276 F.3d 1368 (Fed. Cir. 2002). In that case, a generic drug maker, Andrx Corp., prevailed in a patent infringement suit brought by Biovail to block the marketing of a generic version of Tiazac. This lawsuit had triggered a 30-month stay under the

Hatch-Waxman Amendments. As the first 30-month stay was about to expire and as Andrx was to begin marketing generic Tiazac, Biovail listed a new patent (the "'463 patent") in the Orange Book that Biovail alleged claimed the approved Tiazac, thereby triggering another 30-month delay in the availability of the lower-priced, generic alternative.

The '463 patent, however, did not claim the formulation of Tiazac that was described in Biovail's approved NDA and therefore was ineligible for listing in the Orange Book. In fact, *FDA itself* concluded that the '463 patent did not meet the statutory criteria for listing, stating in a court document that "the '463 patent does not claim the approved drug product as required by [the FFDCA] and therefore cannot be listed in the Orange Book for Tiazac." *Andrx Pharm. Inc. v. Biovail Corp. Int'l*, No. 01-6194- civ – Dimitrouleas/Johnson (S.D. Fla.) (Federal Defendants' Notice of Change in Position, at 3) (February 28, 2001). Although the Agency subsequently attempted to revise this statement and to argue that it did not review Orange Book listings, it also concluded that the newly patented product would require a supplemental new drug application, which demonstrates beyond any doubt that the '463 patent did not claim the approved product. Thus, the determination as to whether the Orange Book listing was appropriate did not involve issues of patent validity, but only required FDA to determine the scope of an approved drug – an issue directly within the Agency's area of expertise. Nevertheless, FDA declined to delist the '463 patent and instead simply accepted Biovail's representation that it met the listing criteria – a representation later sanctioned by the FTC as being false.

An effective patent listing review mechanism need not involve FDA in the direct review of patents' scientific bases. As discussed above, the Agency has, as part of its proposed rule, put forth a revised, expanded declaration that proponents of an Orange Book listing must submit in order to demonstrate that they meet the listing criteria. This declaration is intended to make

listing proponents more accountable and more aware of the listing criteria; it can also, however, provide FDA with a basis for refusing to list a patent if, on the face of the declaration, the patent is not eligible for listing. In GPhA's view, the expanded declaration is not perfect; however, GPhA strongly supports the concept of an expanded declaration and believes that such a declaration can obviate some of the concerns FDA has expressed about its ability to address listing disputes.

In short, whether a patent should be listed or delisted is often not a question of patent *validity* or patent *infringement*, but rather whether the patent meets the listing criteria of the FFDCA and FDA's regulations. The Agency should not continue to abdicate its responsibility to determine whether a patent satisfies requirements that are set forth *in the Agency's own regulations and in its governing statute.* A viable Orange Book listing review mechanism is an essential part of any FDA Hatch-Waxman reform effort.

VI. THE 30-MONTH STAY PROVISION

FDA's proposed rule limits the number of 30-month stays available to a brand company to one stay per ANDA. GPhA applauds FDA's recognition that brand companies have manipulated the 30-month stay provisions to delay access to affordable versions of important drug products and concurs with the Agency's conclusion that Congress never intended to permit such manipulation. The proposed rule, however, is problematic for two reasons. First, the proposed rule may undermine the very goals it purports to advance by making less likely the timely resolution of patent disputes between brand and generic companies. Second, the rule is likely to face, and may not withstand, a court challenge.

A. The Proposed 30-Month Stay Provision Would Delay the Resolution of Patent Disputes and Could Undermine the Goal of Ensuring Timely Access to Affordable Pharmaceuticals.

FDA's proposed limitation on 30-month stays, while well-intentioned, could actually undermine the goal of increasing the public's access to affordable versions of important drug products. The proposal would modify the 30-month stay provisions without taking full account of the vital role the stay plays in the overall Hatch-Waxman system and without adopting other provisions to compensate for the reduced role that FDA contemplates for the stay in its amended regulations.

As discussed in Section III, one of the ways Hatch-Waxman achieves its goal of increased public access to generic drugs is by providing for the early litigation of legitimate patent disputes between brand and generic companies. Early litigation and resolution of these patent disputes gives generic companies the certainty they need before they can go to market.

As also discussed above, it is the *30-month stay* that gives brand companies the incentive under the current system to submit to Hatch-Waxman's expedited patent resolution procedures. The 30-month stay gives the brand company an additional two and one-half years of market exclusivity beyond what it receives under the patent laws and therefore confers enormous financial windfalls on those companies that receive it. But a brand company is entitled to such a stay *only* if it (1) lists a patent in the Orange Book *and* (2) timely files suit after the generic company notified the brand company of its Paragraph IV certification to that patent. Hatch-Waxman does not require brand companies to bring suit on their patents at the time of a Paragraph IV certification; and while FDA may withdraw NDAs for failure to list eligible patents in the Orange Book, the Agency has indicated that it will not do so. The *only* reason brand companies today list patents in the Orange Book and file infringement suits against generic

companies soon after receiving notice of a Paragraph IV certification is because of the availability of the 30-month stay.

The proposed rule removes the incentive of the 30-month stay in certain instances but fails to replace it with a carrot or stick to encourage brand company participation in the Hatch-Waxman system. If FDA's proposed rule were finalized in its current form and the scope of the 30-month stay provisions were narrowed, without any additional changes to the current system, brand companies would have little or no incentive either to list certain patents in the Orange Book, or to initiate litigation on those patents at the beginning of the ANDA approval process. In fact, brand companies clearly understand that, given the availability of lost-profits damages, generics need clarity before launching products. And absent any reason to act otherwise, brand companies would quickly adopt a new strategy to delay generic market entry: sue on the 30-month stay patent, but delay listing or suing on remaining patents until after the expiration of the 30-month stay. By delaying suit until the generic company is ready to launch, the brand companies could introduce an entirely new element of uncertainty and risk into the complex investment and marketing calculations that generic companies must make. Even a generic company that after several years had prevailed in patent infringement litigation could not launch its product without risking infringement damages from patents that had not been subject to early litigation triggered by the incentive of the 30-month stay.

In short, GPhA is concerned that brand companies will use the proposed rule, which the Agency intends to be a way of speeding generic market entry, to *delay* competition. And the longer brand companies are permitted to delay litigation of legitimate patents that are ineligible for 30-month stays, the longer this nation's healthcare system may have to endure monopoly brand drug prices.

The legal analysis that FDA relies on to support its proposed limitation on 30-month stays creates additional problems by calling into question a generic company's ability to force early litigation of brand company patents. Specifically, FDA proposes to limit brand companies to one 30-month stay by narrowly interpreting the Paragraph IV notice requirements of Hatch-Waxman. 67 Fed. Reg. at 65455. Under current law, this notice triggers the availability of the 30-month stay provisions, which in turn gives the brand company an incentive to sue the generic early. FDA, however, has now determined that in certain instances, such notice is not required, and therefore the 30-month stay is not available, under the statute. As GPhA understands FDA's interpretation, a generic company may not even provide formal notice under the statute of its Paragraph IV certification on a voluntarily basis, in order to make a 30-month stay available to a brand company and thereby prompt early litigation of a patent dispute.[15]

Further, FDA's reliance on the notice provisions might also affect a generic company's ability to initiate early litigation of a patent through the commencement of a declaratory judgment action. A generic company may, under current law, have the right to bring such an action if a brand company chooses not to sue for infringement.[16] Under section 505(j)(5)(B)(iii)(III) of Hatch-Waxman, 21 U.S.C. § 355(j)(5)(B)(iii)(III), the generic can bring such an action only if the patentee fails to bring an infringement action within 45 days of *receiving the generic company's Paragraph IV certification notice letter*. GPhA would assert

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[15] As discussed above, at n. 4, should FDA finalize the proposed rule in its current form, GPhA members urge the Agency to adopt an interpretation of the rule that will permit, but not require, generic applicants to provide brand companies with a notice that can trigger a 30-month stay.

[16] Even under the current system, declaratory judgment actions by generic applicants are far from certain. Such actions can be dismissed by the courts for lack of "case or controversy" when the generic cannot meet the subjective standard of proving a reasonable apprehension of a suit by the brand company. *See Cordis Corp. v. Medtronic, Inc.*, 835 F.2d 859, 862 (Fed. Cir. 1987).

that, under FDA's proposal (where notice is neither required nor even perhaps permitted), there would be no temporal limitation on a generic company's filing of a declaratory judgment action. Given the financial stakes, one can expect, however, that a brand company will argue that the absence of a notice period actually divests the generic company of any right to bring a declaratory judgment action at all. FDA's legal justification for its proposed rule adds an unwanted element of uncertainty to this already murky legal area.

The FDA proposal might also have unintended adverse effects on the 180-day exclusivity provision (21 U.S.C. § 355(j)(5)(B)(iv)) – the principal incentive for generics to challenge and remove the barriers caused by questionable brand company patents. As noted above, the incentives created by the proposed rule will significantly delay patent litigation on later-issued patents. In many cases, such litigation will not occur until after generic drug approval, and possibly after the 30-month stay litigation is resolved. This will inject a new level of complexity into a statutory provision that FDA has struggled to implement in a manner that courts consider to be consistent with the statute. For example, the issue of "triggering" events will be complicated when additional litigation occurs late in the process and separate from the initial patent litigation. Likewise, some generic companies could lose some or all of their exclusivity when other generic applicants (that filed a paragraph IV certification but were not sued by the brand company) receive a rapid declaratory judgment for the same patent on jurisdictional grounds. *See Teva Pharm. USA, Inc. v. FDA*, 182 F.3d 1003 (D.C. Cir. 1999) (holding that a declaratory judgment where the brand company admits non-infringement triggers the exclusivity). At the very least, one can expect that delaying the litigation of brand company patents significantly increases the probability of a delay in the triggering event for 180-day

exclusivity, which will in turn delay the operation of the exclusivity and ultimately delay the availability of FDA-approved affordable generic drugs.

In short, both the FDA's proposed limitation of 30-month stays and the Agency's supporting legal reasoning compound the uncertainties facing generic companies and therefore are at odds with the overall goals of Hatch-Waxman. GPhA cannot predict other ways in which brand companies will attempt to manipulate any new Agency regulations, but it is certainly possible that the proposed rule will have further unintended adverse effects on the Hatch-Waxman balance.

These criticisms are not intended to call into question the value of what FDA is trying to accomplish in its proposed rule. As FTC and FDA have both recognized, the availability of multiple 30-month stays has enabled brand companies to game the current Hatch-Waxman system. Eliminating this gaming is an important objective of any reform effort. As we discuss above, another vehicle for Hatch-Waxman abuse is the Orange Book listing process, and GPhA also urges FDA to establish a delisting process that will prevent brand companies from gaming the system through the listing of frivolous patents in the Orange Book.

Nevertheless, measures to limit abuse of the Hatch-Waxman system need not undercut provisions to ensure that brand companies list eligible patents in the Orange Book and initiate early litigation against ANDA applicants with Paragraph IV certifications. FDA's effort to solve the problem of gaming of the 30-month provisions suffers from precisely this flaw and in the end may actually undermine the ability of generic companies to resolve patent disputes as early as possible. Consequently, GPhA does not endorse this portion of the proposed rule and urges FDA to withdraw it.

In summary, there are ways of reconciling the twin goals of preventing gaming of the Hatch-Waxman system and ensuring early resolution of patent disputes. For instance, bills introduced in the 107th Congress would have limited the scope of the 30-month stay provisions to litigation involving patents that were listed no later than 30 days after the original brand company NDA and would therefore have encouraged brand company participation in the Hatch-Waxman process.[17] Specifically, these bills required brand companies to list eligible patents in the Orange Book or to forfeit the right to enforce those patents at all. The bills also required brand companies to sue a generic ANDA applicant with a Paragraph IV certification within the 45-day notice period – regardless of whether the certification could give rise to a 30-month stay – or lose the right to sue to enforce that patent, inside or outside the Hatch-Waxman system. Thus, recent legislative vehicles, unlike the proposed rule, have coupled limitations on the 30-month stay with viable patent listing and litigation incentives.[18]

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[17] This approach is preferable to the Agency's approach, which limits the 30-month stays to patents listed prior to the first generic ANDA filing that contains a paragraph IV certification. The Agency's approach does not address the use of later-issued patents to obtain 30-month stays when the first listed patents remain unchallenged (*i.e.*, when the original submission contained a paragraph I, II, or III certification to each patent). Specifically, the proposed rule, unlike the legislative proposals, does not prevent a brand company from filing frivolous patents for the purpose of obtaining *a first* 30-month stay. The recent increase in patent challenges largely has been due to an increase in the number of patents listed in the Orange Book long after the initial NDA approval and after the filing of the generic ANDA. The Agency's proposal, therefore, does nothing to preclude brand companies from delaying generic competition by listing a frivolous patent later in the ANDA review process and shortly before the first listed – unchallenged -- patent(s) expires.

[18] Another way of ensuring that patents are litigated in the Hatch-Waxman system is to provide that a generic company may sue for a declaratory judgment on the validity or infringement of a patent if a brand company declines to prosecute its own suit within a specified period of time. This mechanism was also included in some of the bills introduced in the 107th Congress, such as Senate Bill 812 that passed 78-21.

The coupling of these two types of Hatch-Waxman reforms is necessary to restore the original statutory balance. Whether *FDA* has the statutory authority to take a comprehensive approach to reform is, however, in doubt. For this reason, GPhA continues to maintain that comprehensive legislative reform of Hatch-Waxman is the only way to address the system's current imbalance and will urge the 108th Congress to enact legislation that contains both meaningful anti-gaming provisions (*i.e.,* limitations on the 30-month stay and a viable delisting procedure for frivolous patents) *and* meaningful incentives to ensure the early resolution of patent disputes.

B. The 30-Month Stay Provision Will Likely Face, and May Not Survive, a Court Challenge.

FDA's 30-month stay proposal faces an additional problem: it will likely face, and may not survive, a court challenge. Such a challenge will probably be brought by a brand company that seeks a second 30-month stay to extend its product monopoly beyond the duration of its patent rights.

As FDA acknowledges in its Federal Register notice, it has repeatedly rejected arguments by GPhA, GPhA's members, and others that Hatch-Waxman can be read to limit the number of 30-month stays available per ANDA. Indeed, the Agency has expressly endorsed the contrary position, arguing in court that it lacks statutory authority to limit the scope of the 30-month stay provisions, and apparently it intends to continue to advance this argument until the proposed rule is finalized. For example, in *Andrx Pharmaceuticals, Inc. v. Biovail Corp.*, No. 01-6194-civ-Dimitrouleas/Johnson (S.D. Fla.) (Memorandum of Federal Defendants in Opposition to Plaintiff's Motion for Summary Judgment Declaring Additional 30-Month Stay Inapplicable or Eliminated, at 5), FDA stated unequivocally that the Hatch-Waxman 30-month stay provisions "[are] not rendered inapplicable to a patent newly listed in the Orange Book simply because the

holder of the NDA has already received the benefit of such a stay with respect to a previously listed patent for the same drug."

The position taken by the Agency on 30-month stays in the proposed rule is an abrupt about-face from its previous statutory interpretation. Moreover, the Agency continues to reject alternative analyses in support of limiting the 30-month stay provisions and instead relies on a textual interpretation of the Hatch-Waxman Act that to GPhA's knowledge has never before been advanced in any forum by any party. FDA's proposed rule, if finally approved, is likely to face a legal challenge by a brand company with a financial interest in obtaining a second 30-month stay. Such a challenge could be successful, and if so would leave the Hatch-Waxman system where it is now – in disrepair.

There are several potential problems with the Agency's analysis of the 30-month stay provisions. First, as noted above, FDA's general position that the Hatch-Waxman Act can be read to limit the number of 30-month stays per ANDA is a 180-degree reversal of the Agency's longstanding position that it *could not* limit the number of 30-month stays. "[A]n agency interpretation of a relevant provision which conflicts with the agency's earlier interpretation is 'entitled to considerably less deference' [under *Chevron, U.S.A., Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837 (1984)] than a consistently held agency view." *INS v. Cardoza-Fonseca*, 480 U.S. 421, 446 n. 30 (1987), *quoting Watt v. Alaska*, 451 U.S. 259, 273 (1981). Even if reversals of long-held Agency positions were entitled to some deference under *Chevron*, the Agency bears the burden of articulating a rational basis for its change of policy. *Motor Vehicle Mfr. Ass'n v. State Farm Mut. Auto*, 463 U.S. 29, 41-44 (1983). It could be argued that while the Agency's Federal Register Notice presents a rational reason for FDA's change of position – that is, the increase in the number of 30-month stays -- this increase has

been occurring for several years and the Agency has nevertheless consistently rejected arguments that it change its legal interpretation of the statute.

Second, it could be argued that, in any event, FDA's textual interpretation of the Hatch-Waxman Act does not support its new interpretation of the statute, and should not be given *any* deference under *Chevron*. 467 U.S. at 840 (agency interpretation entitled to no deference where Congress spoke directly to the issue and statutory text admits of only one plain meaning). The proposed rule's 30-month stay analysis hinges on FDA's interpretation of the verb "include." Under section 505(j)(2)(B)(iii) of the FFDCA, 21 U.S.C. 355(j)(2)(B)(iii), a generic company must notify a brand company when the generic ANDA is "amended to include" a Paragraph IV certification. Such notice, in turn, triggers the brand company's right to a 30-month stay. FDA's argument, on which its entire analysis depends, is that an ANDA that is changed to add a *second* Paragraph IV certification has not been "amended to include" a Paragraph IV certification because the original ANDA already contained an earlier Paragraph IV certification. In such cases, therefore, notice to the brand company of the new Paragraph IV certification is not required and a 30-month stay based on the later-issued patent is not available. In other words, FDA reads the word "include" to mean "include for the first time" and thereby limits the number of stays available per ANDA. 67 Fed. Reg. at 65455.

This analysis will surely be questioned in any judicial challenge to the rule. First, the verb "include" arguably does not mean "include for the first time," but rather means "contain." *See American Heritage Dictionary* (1980 ed.) at 665; *Chickasaw Nation v. United States*, 534 U.S. 84, 89 (2001) (defining "include" to mean "to contain."). And an ANDA that contains a Paragraph IV certification added by amendment probably "includes" or "contains" that certification *regardless of* whether another Paragraph IV certification preceded it. While FDA's

interpretation would likely hold up if Hatch-Waxman contemplated the presence of only one Paragraph IV certification per ANDA, the statute appears to contemplate, and provide for, the presence of several such certifications per ANDA. In this context, it could be argued that the word "include" cannot be interpreted to impose a limitation on what came before the included item, and that a Paragraph IV certification can be "included" in an ANDA even if another, different Paragraph IV certification is already in that ANDA.

A brand company seeking a second 30-month stay is also likely to take the position that any other reading of the statute would be inconsistent with the intent of Hatch-Waxman. The statute specifically requires a separate certification for each listed patent in order to identify and expedite the resolution of *any* – not just the first -- potential patent disputes. In addition to triggering a potential 30-month stay, this notice informs the generic company of the identity of outstanding patents. A reading of the statute that short-circuited the identification of patent disputes for later-issued patents would be in conflict with Congress' goals.

The courts have not hesitated to strike down Agency interpretations of the FFDCA that it deemed unsustainable, even where such interpretations were driven by broad public policy objectives and even with full *Chevron* deference due the Agency. *E.g., Ass'n of Am. Physicians and Surgeons, Inc. v. FDA*, Civ. No. 00-02898 (HHK) (October 17, 2002) (striking down FDA pediatric rule). *See also Mova Pharmaceutical Corp. v. Shalala*, 955 F.Supp. 128 (D.D.C. 1997) (eliminating the "successful defense" requirement for 180-day exclusivity); *Mylan Pharms., Inc. v. Shalala*, 81 F.Supp. 2d 30 (D.D.C. 2000) (striking down FDA definition of "court" for purposes of 180-day exclusivity). Litigants may argue that the proposed 30-month stay rule should face a similar fate, especially since the rule may not be entitled to full *Chevron* deference.

VII. CONCLUSION

For the foregoing reasons, GPhA urges FDA to:

(1) Adopt the part of its proposed rule that clarifies that patent claiming metabolites, packaging and intermediates cannot be listed in the Orange Book;

(2) Adopt the part of its proposed rule that creates a new patent listing declaration, but with additional questions relating to product-by-process patents;

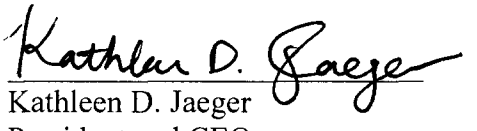
(3) Withdraw from its proposed rule the requirement that product-by-process patents be listed in the Orange Book;

(4) Withdraw from its proposed rule the requirement that polymorph patents be listed in the Orange Book;

(5) Adopt a meaningful Orange Book delisting process as part of its proposed rule; and

(6) Withdraw the section of its proposed rule relating to 30-month stays.

Respectfully submitted,



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